

# A Clinicopathological Study in Young Patients with Gastric Carcinoma

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**Background and Objectives:** Gastric carcinoma rarely affects young patients. This study was undertaken in order to clarify the clinicopathological features and prognosis of young patients with gastric carcinoma.

**Methods:** The resected 107 specimens from 105 patients younger than 30 years of age with gastric carcinoma were investigated using hematoxylin and eosin stain.

**Results:** The male:female ratio was 1:1.6. Histologically, poorly differentiated adenocarcinoma was the most common type (94/107, 87.9%) ( $P < 0.001$ ). Most tumors were located in the middle third of the stomach ( $P < 0.001$ ). All patients had depressed lesions. The 5-year survival rates of early and advanced gastric carcinoma were 100% (30/30) and 23.5% (8/34), respectively.

**Conclusions:** Characteristic clinicopathological features in young patients, such as gender ratio, tumor location, macroscopic type, and histological type, were different from those in older ones. The prognosis of early gastric carcinoma in young patients was much better than that in older patients, although the prognosis of advanced gastric carcinoma in young patients was worse than that of older patients. These findings seem to indicate that young patients with early gastric carcinoma can tolerate radical treatments well; however, the aggressiveness of lesions are emphasized in patients with advanced gastric carcinoma.

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**KEY WORDS:** ulcerating infiltrative; male:female ratio; adenocarcinoma; differentiation

## INTRODUCTION

Gastric carcinoma is a common disease that usually affects older patients, rarely affecting younger patients. It has been estimated that patients younger than 40 years of age represent between 2–8% of all the patients with gastric carcinoma [1,2]. There have been several previous reports of gastric carcinoma in patients younger than 30, 35, 36, 39, or 40 years [3–10] and case reports of patients younger than 30 [11,12] years and, in particular, in children [13–17]. However, the prognosis in young patients has shown considerable variability, with a delay in diag-

nosis due to the lack of severe symptoms and with a more aggressive course of the disease in these age groups. In this study, we present the clinicopathologic analysis of gastric carcinoma in 105 patients younger than 30 years old.

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## MATERIALS AND METHODS

### Materials

The clinicopathological features of 105 young patients (defined as younger than 30 years of age) with gastric carcinoma from the Second Department of Pathology, Faculty of Medicine, Kyushu University (Fukuoka, Japan) and from its affiliated hospitals were reviewed retrospectively for the period 1963 to 1997. The resected tissue specimens were fixed in 10% buffered formalin and embedded in paraffin. Histologic sections cut from paraffin blocks were stained routinely with hematoxylin and eosin. In our country, early gastric carcinoma, which is defined as carcinoma confined to the mucosa or mucosa and submucosa, regardless of the presence of lymph node metastasis, as macroscopically divided as follows. That is, protruded (type I), elevated (type IIa), flat (type IIb), depressed (type IIc), excavated (type III), and unclassified type. For early gastric carcinomas with a combination of features, the dominant pattern is regarded as the representative macroscopic type. On the other hand, advanced gastric carcinoma is classified by means of Borrmann's classification. That is, polypoid (Borr.1), ulcerated (Borr.2), ulcerating infiltrative (Borr.3), diffusely infiltrative (Borr.4), and unclassified type.

### Statistical Analysis

The survival rates of the patients were calculated using the Kaplan-Meier method, and statistical differences were calculated with the use of the generalized Wilcoxon test. Other statistical differences were evaluated by the chi-square and Student's *t*-test. *P* values were derived from two-tailed tests. A *P* value of less than 0.05 was considered to be statistically significant.

## RESULTS

### Clinical and Histopathological Findings

The young patients with gastric carcinoma consisted of 40 males and 65 females. The age of the patients at the time of the initial diagnosis ranged from 7 to 30 years, with a mean age of 26.7 years. The youngest patient was a 7-year-old boy, whose case had been reported previously [13], and two teenagers were also included in this study.

In Japan, it has been proposed that gastric carcinoma should be classified microscopically by the depth of invasion into the following two types: early, carcinoma confined to the mucosa or submucosa; advanced, carcinoma invading beyond the muscularis propria.

Table I summarizes the clinicopathological findings of early and advanced gastric carcinoma in young patients. Of 105 patients, double early gastric carcinomas were encountered coincidentally in two patients. Among the 107 lesions, 5 lesions were located mainly in the upper third of the stomach, 74 in the middle third, 24 in the

TABLE I. Clinicopathological Findings of Early and Advanced Gastric Carcinoma in Young Patients\*

	Early (47 lesions)	Advanced (60 lesions)
Age (yr)	26.4	25.8
Gender (male:female)	17:28	23:37
Site of tumor (C:M:A:C-A)	1:35:11:0	4:39:13:4
Size of tumor (cm)	3.5	6.9
Macroscopical type (IIc:IIc+III:IIc+IIa) (Borr2:Borr3:Borr4:unclassified)	33:12:2	2:44:7:7
Histological type (well:mod:poor:sig)	1:5:35:6	1:6:50:3
Depth of invasion (m:sm:mp:ss:se)	19:28:0:0:0	0:0:7:40:13
Lymphatic invasion (-: +)	38:9	23:37
Venous invasion (-: +)	45:2	50:10
Surgical margin (-: +)	46:1	56:4
Lymph node metastasis <sup>a</sup> (-: +)	22:3	12:21

\*C, upper portion of the stomach; M, middle; A, lower; C-A, whole; IIc, depressed type; III, excavated type; IIa, elevated type; Borr 2, ulcerated type; Borr 3, ulcerating infiltrative type; Borr 4, diffusely infiltrative type; well, well-differentiated adenocarcinoma; mod, moderately differentiated adenocarcinoma; poor, poorly differentiated adenocarcinoma; sig, signet ring cell carcinoma; m, mucosa; sm, submucosa; mp, muscularis propria; ss, subserosa; se, serosa.

<sup>a</sup>Lymph node metastasis that could be ascertained.

lower third, and 4 almost throughout the entire stomach. Differing from our previous study [18], the location of the tumors was significantly more frequent in the middle third than in the lower third (*P* < 0.001).

The majority of early gastric carcinoma in young patients was type IIc (33/47, 70.2%). The remaining, of the unclassified type, exhibited combined type of early gastric carcinoma, consisting of 12 type IIc+III lesions and 2 type IIc+IIa lesions.

The most common type of advanced gastric carcinoma in young patients was ulcerating infiltrative type (44/60, 73.3%). Seven lesions were of the diffusely infiltrative type (7/44, 15.9%).

Of the 107 lesions of gastric carcinoma, 2 were classified as well differentiated adenocarcinoma, 11 as moderately differentiated adenocarcinoma, 85 as poorly differentiated adenocarcinoma, and 9 as signet-ring cell carcinoma. The degree of the depth of tumor invasion into the gastric wall was as follows: 19 of 107 lesions were restricted to the mucosa, 28 confined to the submucosa, 7 involved the muscularis propria, 40 involved all the layers of the gastric wall, including to the subserosa, and 13 had penetrated beyond the serosa. Figure 1 shows macroscopic and microscopic pictures of a typical case of early gastric carcinoma in the present study, and Figure 2 shows those of a typical case of advanced gastric carcinoma.

Macroscopic and histological findings in relation to 5-year survival rates in 64 cases in which we were able to investigate prognosis are shown in Tables II and III. All the young patients had depressed lesions. No polypoid lesions were seen, neither in early nor advanced gas-

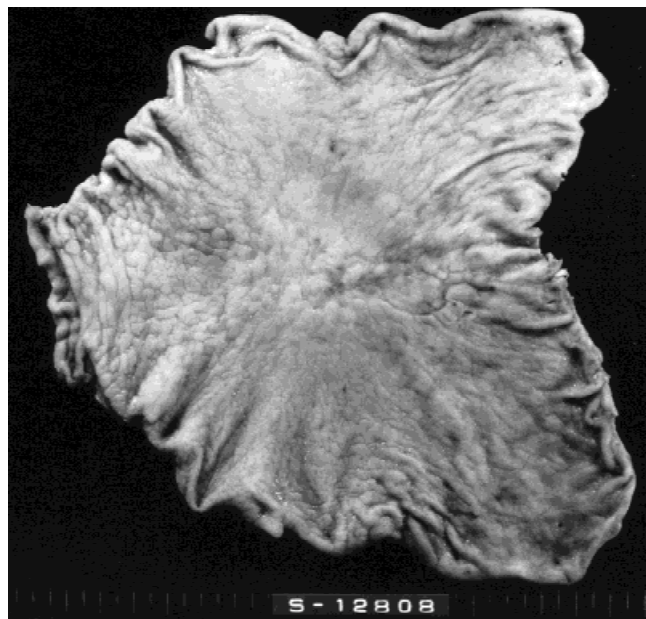


Fig. 1. Early gastric carcinoma in a 30-year-old female. Macroscopic picture of Ic type. A shallow depressed and well-demarcated ulceration with a granular surface.

tric carcinoma. The majority of early gastric carcinoma in young patients was type Ic (23/30, 76.7%). The remaining 7 were type Ic+III.

On the other hand, among young patients with advanced gastric carcinoma, the most common type was ulcerating infiltrative type (Borr.3) (28/34, 82.4%). Only 3 lesions were of the diffusely infiltrative type (Borr.4) (3/34, 8.8%).

The overall 5-year survival rate of 64 cases in which we were able to investigate prognosis was 48.5% (38/64). In 30 cases of early gastric carcinoma in young patients, a significantly better prognosis ( $P < 0.001$ ) was noted compared with advanced gastric carcinoma in young patients; the 5-year survival rate of early gastric carcinoma was 100% (30/30) and that of advanced gastric carcinoma was 23.5% (8/34) (Fig. 3).

There was no difference between clinicopathological findings and 5-year survival rates in young patients with early gastric carcinoma with respect to gender, age, type of operation, tumor location, size, macroscopic type, histological type, depth of invasion, surgical margin, and lymph node metastases (Table II).

Table III shows clinicopathological findings and 5-year survival rates in young patients with advanced gastric carcinoma. The 5-year survival rate of males was 20.0% (3/15) and that of females was 26.3% (5/19). Of 29 patients who underwent subtotal gastrectomy, 8 patients survived for 5 years (27.6%). Of the patients who underwent total gastrectomy or fundic resection, none were able to survive. Forty percent (8/20) of the patients

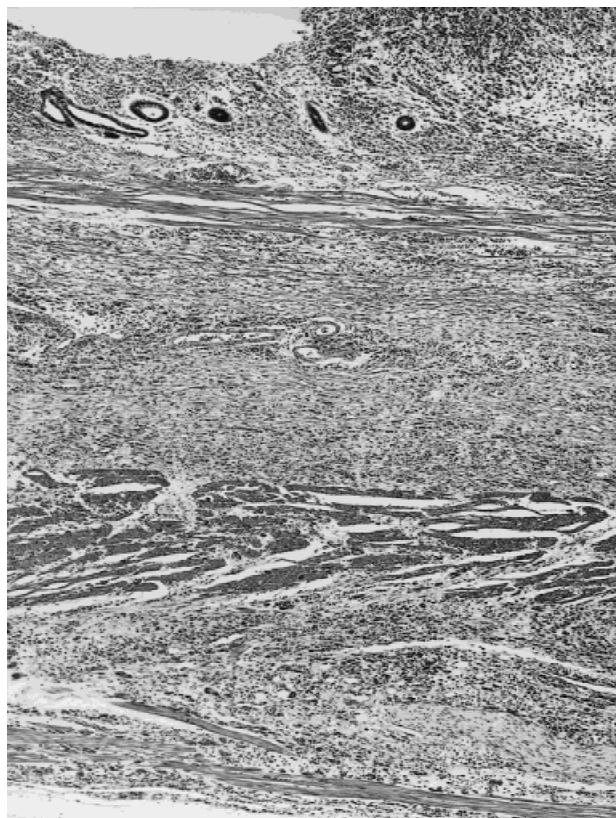


Fig. 2. Advanced gastric carcinoma in a 30-year-old female. Low-power histologic pictures show poorly differentiated adenocarcinoma with signet-ring cells proliferating in a scirrhous fashion and invading the whole thickness of the gastric wall (H&E, original magnification  $\times 22$ ).

with gastric carcinoma arising in the middle third of the stomach could survive for 5 years. All the patients who survived for 5 years had ulcerating infiltrative type of gastric carcinoma (8/28, 28.6%). One of 3 patients with moderately differentiated adenocarcinoma (33.3%) and seven of 30 patients with poorly differentiated adenocarcinoma (23.3%) survived for 5 years. The 5-year survival rate varied in the depth of invasion: mp (muscularis propria), 25.0% (1/4); ss (subserosa), 26.9% (7/26); and se (serosa), 0% (0/4). The surgical margins of the patients who survived for 5 years were free of carcinoma cells, although all of the surgical margins of those who died within 5 years were positive for carcinoma cells. The 5-year survival rate of young patients with lymph node metastases was 7.1% (1/14) and that of young patients without lymph node metastases was 42.9% (3/7).

## DISCUSSION

Gastric carcinoma is usually a disease of the aged with patients showing a mean age of approximately 50–60 years [3,5]. In the present study, only 1.07% (105/9,772) of all patients with this disease registered in the Second



**TABLE II. Clinicopathological Findings With Survival Rates of Early Gastric Carcinoma in Young Patients\***

	No. of patients (%)	Survival rate (5 year; %)
Total no.	(n = 30)	100
Gender		
Male	7 (23.3)	100
Female	23 (76.7)	100
Age (yr) mean	27.4	
Type of operation		
Subtotal gastrectomy	29 (96.7)	100
Total gastrectomy	0 (0)	—
Fundic resection	1 (3.3)	100
Site of tumor		
C: Upper third	1 (3.3)	100
M: Middle third	23 (76.7)	100
A: Lower third	6 (20)	100
C-A: Whole	0 (0)	—
Size of tumor		
Mean (cm)	3.7	
Range (cm)		
<0.5	0 (0)	—
0.6–2.0	3 (10)	100
2.1–5.0	17 (56.7)	100
5.1–10.0	10 (33.3)	100
10<	0 (0)	—
Macroscopic type		
Protruded (type I)	0 (0)	—
Elevated (type IIa)	0 (0)	—
Flat (type IIb)	0 (0)	—
Depressed (type IIc)	23 (76.7)	100
Excavated (type III)	0 (0)	—
Unclassified	7 (23.3)	100
Histological type		
Well	0 (0)	—
Moderately	2 (6.7)	100
Poorly	28 (93.3)	100
Depth of invasion		
m	13 (43.3)	100
sm	17 (56.7)	100
Surgical margin		
Positive	0 (0)	—
Negative	30 (100)	100
Lymph node metastasis (n = 14)		
Positive	3 (21.4)	100
Negative	11 (78.6)	100

\*m: mucosa; sm: submucosa.

Department of Pathology, Faculty of Medicine, Kyushu University, were younger than 30 years of age. It has been a controversial issue as to whether gastric carcinoma in young patients differs from gastric carcinoma in older patients. We succeeded to investigate the larger number of patients with gastric carcinoma younger than 30 years old that have ever been reported. Mori et al. [5] investigated 23 patients with early gastric carcinoma and reported female predominance (the male:female ratio was 1:2.8). In our previous study [18], a male predominance was found of about 1:0.57 (4,471:2,560). The present study revealed the female predominance in both early and advanced gastric carcinoma. In this study, the overall

**TABLE III. Clinicopathological Findings With Survival Rates of Advanced Gastric Carcinoma in Young Patients\***

	No. of patients (%)	Survival rate (5 year; %)
Total no.	(n = 34)	23.5
Gender		
Male	15 (44.1)	20.0
Female	19 (55.9)	26.3
Age (yr) mean	26.8	
Type of operation		
Subtotal gastrectomy	29 (85.3)	27.6
Total gastrectomy	3 (8.8)	0
Fundic resection	2 (5.9)	0
Site of tumor		
C (Upper third)	2 (5.9)	0
M (Middle third)	20 (58.8)	40.0
A (Lower third)	9 (26.5)	0
C-A (Whole)	3 (8.8)	0
Size of tumor		
Mean (cm)	7.0	
Range (cm)		
<0.5	0 (0)	—
0.6–2.0	1 (2.9)	100
2.1–5.0	12 (35.3)	33.3
5.1–10.0	15 (44.1)	6.7
10<	6 (17.7)	33.3
Macroscopic type		
Polypoid	0 (0)	—
Ulcerated	1 (2.9)	0
Ulcerating infiltrative	28 (82.4)	28.6
Diffusely infiltrative	3 (8.8)	0
Unclassified	2 (5.9)	0
Histological type		
Well	1 (2.9)	0
Moderately	3 (8.8)	33.3
Poorly	30 (88.3)	23.3
Depth of invasion		
mp	4 (11.8)	25.0
ss	26 (76.4)	26.9
se	4 (11.8)	0
Surgical margin		
Positive	3 (8.8)	0
Negative	31 (91.2)	25.8
Lymph node metastasis (n = 21)		
Positive	14 (66.7)	7.1
Negative	7 (33.3)	42.9

\*mp: muscularis propria; ss: subserosa; se: serosa.

male:female ratio was 1:1.6. Thus, a significant gender difference ( $P < 0.001$ ) was recognized between the present study and our previous study [18].

In this study, most tumors were located in the middle third of the stomach in both early and advanced gastric carcinoma (74/107, 69.2%). In early gastric carcinoma, Mori et al. [5] reported the same tendency: middle third, 17; lower third, 6. However, in advanced gastric carcinoma, Wang et al. [2], Choi et al. [9], and our previous study [18] reported a lower third predominance in tumor location.

Macroscopically, a significant difference was recognized between the present study and our previous study

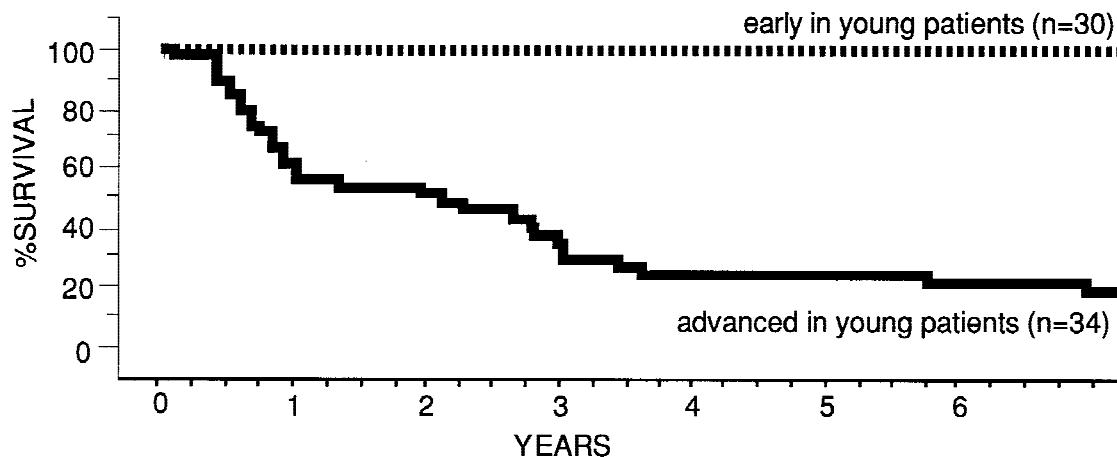


Fig. 3. Cumulative survival rates in early and advanced gastric carcinoma in young patients.

[18] in the ratio of ulcerating infiltrative type (Borr.3) among advanced gastric carcinoma (the present study: 73.3%, our previous study: 41.4%) ( $P < 0.001$ ).

Histologically, poorly differentiated adenocarcinoma was the most common type (94/107, 87.9%) in both early (35/47, 74.5%) and advanced gastric carcinoma (50/60, 83.3%). In our previous study [18], which analyzed pathology and prognosis of gastric carcinoma in 7,031 patients in which the majority were older, 45.5% (1,440/3,163) of early gastric carcinoma was well differentiated adenocarcinoma, 17.4% (550/3,163) of them was moderately differentiated adenocarcinoma, and 37.1% (1,173/3,163) of them was poorly differentiated adenocarcinoma, although the most common histological type was poorly differentiated adenocarcinoma in advanced lesions (2,186/3,868, 56.5%). A significant difference was recognized between the present study and our previous study [18] in histological type ( $P < 0.001$ ).

The majority of gastric carcinoma in young patients was depressed lesions composed of poorly differentiated adenocarcinoma both in early and advanced stages. In early gastric carcinoma, this was also found in the study done by Mori et al. [5]. Wang et al. [2] reported only one polypoid lesion in 21 cases, among patients younger than 40 years. Choi et al. [9] found that no polypoid was found among 91 patients younger than 40 years old. Our previous study [18] reported some correlation between macroscopic and histological type. Ninety-seven percent of diffusely infiltrative tumors and 69% of ulcerating infiltrative tumors were poorly differentiated in advanced carcinomas. Eighty-nine percent of type I and 77% of type IIa showed well-differentiated adenocarcinoma in early carcinomas. The fact that ulcerative lesions are easy to find and protruded lesions are rare in young patients, especially younger than 30 years old, seems to be reasonable.

The prognosis of young patients with gastric carcinoma has shown considerable variation, although it is

generally poorer than or similar to that of older patients [1–4,9]. In young patients, it has traditionally been considered as more aggressive and poorer in their prognosis. However, among young patients with early carcinoma, better a 5-year survival rate (30/30, 100%) was recognized in this study, compared with our previous report [18] (2,808/3,163, 88.8%). Mori et al. [5] reported that the 5-year survival rate of 23 patients with early gastric carcinoma (m: 12, sm: 11) was 100%. The young patients with early gastric carcinoma in this study (m: 13, sm: 17) have also shown a 5-year survival rate of 100% (30/30). Among the young patients with advanced carcinoma, a poorer 5-year survival rate (8/34, 23.5%) was seen in this study, compared with our previous report [18] (1,783/3,868, 46.1%), concerning every clinicopathological aspect. Choi et al. [9] reported that the 5-year overall survival rate of young patients with advanced gastric carcinoma was 51.9% for the patients aged under 35 years and 54.6% for the patients between 36 and 39 years old. These facts seem to indicate that young patients with early gastric cancer can tolerate radical treatments well. However, the aggressiveness of lesions are emphasized in the cases of advanced gastric carcinoma as age decreases.

The comparison between the present study and previous studies [2,5,9,18] leads to the conclusion that the prognosis of advanced gastric carcinoma in young patients is worse than that of advanced gastric carcinoma in older patients. However, the prognosis of early gastric carcinoma in young patients was very good. Therefore, it is important to make a precise diagnosis promptly for gastric carcinoma in young patients and to treat it in the early stage, even though the prevalence of gastric carcinoma among young patients is low.

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